Air pollution has been implicated to be associated with a wide range of early responses in the lung, the circulation and even at more distant organs. Oxidative stress, immune activation, changes in autonomic function and direct impact on various organs has been implicated. The paper will describe the identified modes of actions of ambient air pollution. It will highlight the role of the different physicochemical characteristics of aerosols in inducing systemic responses in humans. In order to further establish the role of the various hypothesised mechanisms, the genomic variability was assessed as potential modifier of the air pollution responses. The paper will review advances made by candidate gene approaches focussing on the cardiovascular system. This evidence will be contrasted with recent advances of genomic control in relevant response-pathways based on genomewide association studies.